

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
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 GERMANY

Eingegangen / Received

20. Jan. 2005 AB

MÜLLER · FOTTNER · STEINECKE

Frist: 08.05.05 bis d.h.

Applicant's or agent's file reference
 AX02A15/P-WO

International application No.
 PCT/EP2004/007530

Applicant

AXIOGENESIS AG

PCT

NOTIFICATION OF TRANSMITTAL OF
 THE INTERNATIONAL SEARCH REPORT AND
 THE WRITTEN OPINION OF THE INTERNATIONAL
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

19/01/2005

Date of mailing
 (day/month/year)

FOR FURTHER ACTION See paragraphs 1 and 4 below

International filing date
 (day/month/year)

08/07/2004

1. The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
 1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
 - the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
 - no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Sabine Oblinger

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference AX02A15 / P - WO	FOR FURTHER ACTION		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/EP2004/007530	International filing date (day/month/year) 08/07/2004	(Earliest) Priority Date (day/month/year) 08/07/2003	
Applicant AXIOGENESIS AG			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. Certain claims were found unsearchable (See Box II).

3. Unity of invention is lacking (see Box III).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. 1

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

- b. none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/007530

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-30, 42-44

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-30, 42-44

Method for producing embryoid bodies based on agitation technique, use of said method for biological assays, the required kit and its use.

2. claims: 31, 41

Embryoid bodies

3. claims: 32-33, 41

Differentiated cells derived from embryoid bodies

4. claims: 34-40, 43-44

Biological test of compounds with embryoid bodies.

5. claim: 42 partly

Use of embryoid body for loss of function assays of specific genes

6. claim: 42 partly

Use of embryoid bodies for gain of function assays of exogenous genes

7. claim: 42 partly

Use of embryoid bodies for developmental analysis of teratogenic / embryotoxic compounds

8. claim: 42 partly

Use of embryoid bodies for pharmacological assays

9. claim: 42 partly

Use of embryoid bodies for microarray systems

10. claim: 42 partly

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of embryoid bodies for establishment of model systems
for pathological cell functions

11. claim: 42 partly

Use of embryoid bodies for induction of selectively
differentiated cells upon application of growth factors

12. claim: 42 partly

Use of embryoid bodies as source for tissue grafts

13. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 for loss of
function assays of specific genes

14. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 for gain of
function assays of exogenous genes

15. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 for
developmental analysis of teratogenic / embryotoxic
compounds

16. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 for
pharmacological assays

17. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 for microarray
systems

18. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 for
establishment of model systems for pathological cell
functions

19. claim: 42 partly

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of the cell or tissue of claim 32 or 33 for induction of selectively differentiated cells upon application of growth factors

20. claim: 42 partly

Use of the cell or tissue of claim 32 or 33 as source for tissue grafts

INTERNATIONAL SEARCH REPORT

International Application No PCT/EP2004/007530

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT
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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/119107 A1 (DANG STEPHEN ET AL) 26 June 2003 (2003-06-26) page 4, column 1 - page 5, column 1 -----	1-30, 42-44
A	WO 01/62899 A (WISCONSIN ALUMNI RES FOUND) 30 August 2001 (2001-08-30) page 3 - page 7 -----	1-30, 42-44
A	KEHAT IZHAK ET AL: "Human embryonic stem cells can differentiate into myocytes with structural and functional properties of cardiomyocytes" JOURNAL OF CLINICAL INVESTIGATION, NEW YORK, NY, US, vol. 108, no. 3, August 2001 (2001-08), pages 407-414, XP002282071 ISSN: 0021-9738 page 408; figure 1 ----- -/-	17-22, 24-30

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

Y document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

& document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

7 September 2004

Date of mailing of the international search report

19.01.2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
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Authorized officer

Friedrich, C

INTERNATIONAL SEARCH REPORT

International Application No PCT/EP2004/007530

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MEYER N ET AL: "A fluorescent reporter gene as a marker for ventricular specification in ES-derived cardiac cells" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 478, no. 1-2, 28 July 2000 (2000-07-28), pages 151-158, XP004337425 ISSN: 0014-5793 page 152, paragraph 3</p> <p>-----</p>	17-22, 24-30
A	<p>HIDAKA KYOKO ET AL: "Chamber-specific differentiation of Nkx2.5-positive cardiac precursor cells from murine embryonic stem cells." FASEB JOURNAL, vol. 17, no. 6, April 2003 (2003-04), pages 740-742 URL, XP002295090 ISSN: 0892-6638 the whole document</p> <p>-----</p>	17-22, 24-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/007530

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 2003119107	A1	26-06-2003	CA 2351156 A1 WO 03004626 A1 EP 1407002 A2	04-01-2003 16-01-2003 14-04-2004
WO 0162899	A	30-08-2001	US 6602711 B1 AU 3849101 A BR 0108436 A CA 2400158 A1 CN 1404526 T EP 1257634 A2 JP 2003523766 T NO 20023949 A NZ 520700 A WO 0162899 A2 US 2004023376 A1	05-08-2003 03-09-2001 25-03-2003 30-08-2001 19-03-2003 20-11-2002 12-08-2003 20-08-2002 30-04-2004 30-08-2001 05-02-2004